

Regulatory Status of Triclosan and Triclocarban in Nonprescription Products

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Presentation Outline

- **Background**
- **Effectiveness studies**
- **Potential risks**
- **Unanswered questions**



What is a Nonprescription Product?

- **Also called over-the-counter (OTC) drugs**
- **Generally have these characteristics:**
 - **Benefits outweigh risks**
 - **Low potential for misuse and abuse**
 - **Used for self-diagnosed conditions**
 - **Can be adequately labeled**
 - **Health practitioners are not needed for the safe and effective use of the product**

Main OTC Products That Contain Triclosan (TCS) or Triclocarban (TCC)

- **Antiseptics**
 - **Antibacterial soaps** (TCC/TCS)
 - **Hand sanitizers** (TCS)
 - **Antibacterial bodywashes** (TCS)
- **Some toothpastes** (TCS)

Active Ingredients Used in Consumer Antiseptics

- Alcohol
- Chloroxylenol (PCMX)
- Quaternary ammonium compounds
 - Benzalkonium chloride
 - Benzethonium chloride
 - Methylbenzethonium chloride
- Triclocarban
- Triclosan

FDA Regulation of OTC Products

- **There is more than 1 process for regulating OTC products**
- **Antibacterial soaps are regulated under the monograph process**
- **TCS-containing toothpaste is regulated under the new drug application (NDA) process**

Comparison of Nonprescription Drug Regulatory Mechanisms

Drug Monograph

- no pre-approval
- ingredient-based
- public
- long process (yrs)

New Drug Application

- pre-approval req'd
- product-based
- confidential
- short process (mos)

Both procedures are driven by scientific data

The FDA Monograph Process

- **Proposed Rule**
 - **Public comment period**
- **Tentative Final Monograph (TFM)**
 - **Public comment period**
- **Final Rule (Final Monograph)**



What Do We Look For?

- OTC drugs must be found to be *generally recognized as safe and effective* [21 CFR 330.10(a)(4)]
- Studies must be adequate and well-controlled (21 CFR 314.126)
- We also look at the risk/benefit ratio

Where Do We Get Our Data?

- **FDA docket (Regulations.gov)**
 - Data is submitted by industry, trade groups, academia, others
 - Submissions are voluntary
 - Both published & unpublished data
 - Information is public
- **FDA's literature search**
 - Published studies

How Do We Evaluate Antiseptic Effectiveness?

- **In Vitro Effectiveness Studies**
 - **Minimum inhibitory conc., time-kill**
- **Clinical Simulation Studies**
 - **Performed in a lab**
- **Clinical Outcome Studies**
 - **Performed in real-life situations (homes, hospitals, schools)**

Clinical Outcome Study Example

- Year-long study in Pakistan
- Compared use of TCC soap, plain soap & no soap (standard practice)
- 300 households per group
- Looked at the rates of respiratory infection (pneumonia), diarrhea, & skin infection (impetigo)

Luby et al. 2005 Lancet 366:225-233



Clinical Outcome Study Example (2)

- **Field workers visited groups weekly**
 - **Recorded symptoms**
 - **Encouraged hand washing & bathing in the 2 soap groups**
- **Children in the 2 soap groups had fewer cases of pneumonia, diarrhea, and impetigo than controls**

Study Interpretation & Limitations

- **Interpretation**
 - **Reduction in disease due to hand washing & bathing with soap (plus hand washing promotion)**
 - **No added benefit from TCC**
- **Limitations**
 - **Possible under-reporting of illness**
 - **Can't attribute effect to hand washing alone**

Concerns About Antiseptics

- **Antiseptic use may contribute to the development of antibiotic resistance**
 - **Bacteria can easily become resistant to some antiseptics after exposure to low levels**
 - **Bacteria use some of the same resistance mechanisms for antiseptics & antibiotics**
 - **Cross-resistance with antibiotics has the potential to occur based on lab studies**

Cross-Resistance in the Laboratory

- Lab studies commonly use:
 - *E. coli*, *Salmonella enterica*, *Staph. aureus*
 - Amp, Chl, Cipro, Ery, Tet
- Studies show cross-resistance to ≥ 1 antibiotic for at least 1 species
- Although the data are variable, cross-resistance does occur in the lab, especially for gram-negative bacteria

Unanswered Questions

- **Are antibacterial soaps (antiseptics) effective for everyday consumer use?**
- **How do environmental antiseptic concentrations relate to lab concentrations?**